

Agraval, U., Qi, N., Stewart, P., Luo, X., Williams, G., Rotchford, A., and Ramaesh, K. (2015) The optimum size of iridotomy to prevent acute angle closure in a uveitic eye: a novel mathematical model application. *Clinical and Experimental Ophthalmology*.

Copyright © 2015 Wiley

A copy can be downloaded for personal non-commercial research or study, without prior permission or charge

Content must not be changed in any way or reproduced in any format or medium without the formal permission of the copyright holder(s)

<http://eprints.gla.ac.uk/104527/>

Deposited on: 30 March 2015

Letter to the Editor

The Optimum Size of Iridotomy to Prevent Acute Angle Closure in a Uveitic Eye: A Novel Mathematical Model Application

Umiya Agraval¹ MBChB
Nan Qi² MSc
Peter Stewart² PhD
Xiaoyu Luo² PhD
Graeme Williams¹ FRCP(Ed)
Alan Rotchford¹ FRCOphth
Kanna Ramaesh¹ FRCOphth

1. Tennent Institute of Ophthalmology, Gartnavel General Hospital, Glasgow, UK
2. Department of Mathematics and Statistics, University of Glasgow, UK

Correspondence to:

Dr Umiya Agraval
Tennent Institute of Ophthalmology
Gartnavel General Hospital
1053 Great Western Road
Glasgow
UK
G12 0YN
umiya.agraval@nhs.net

Conflict/competing interests: No stated conflict of interest
Funding sources: No stated funding sources

The Optimum Size of Iridotomy to Prevent Acute Angle Closure in a Uveitic Eye: A Novel Mathematical Model Application

The failure of neodymium-doped yttrium aluminium garnet (Nd:YAG) peripheral iridotomy (PI) to prevent and relieve primary acute angle closure glaucoma (AACG) has been well documented in the literature and attributed to inadequate size of PI¹. In cases of uveitis and iris bombe associated AACG the failure rate is significantly greater, in the region of 40-61%^{2,3}.

We present a case of a recurrence of AACG in a uveitic patient despite having a patent PI. We believe a much larger PI is required to prevent recurrent episodes of AACG in a uveitic eye. Therefore, we constructed and applied a mathematical model to determine the optimal size of iridotomy and to help understand and modify treatment options.

Case

A 22 year old female presented to the eye casualty with a one day history of a severely painful left eye, headache, nausea and vomiting. Her vision was counting fingers in the left eye and 6/6 in the right (Figure 1a, 2a, b). She attended three weeks ago with a similar episode, treated with Nd:YAG PI. She has a history of left chronic anterior uveitis resulting in raised IOP, which remained stable following insertion of Ahmed valve and cataract surgery, five months prior to her presentation.

Medical therapy was initiated for AACG and a further Nd:YAG laser PI was performed reducing the IOP to 28mmHg. The PI reduced the degree of iris bombe but did not resolve the occlusion of the drainage angle (Figure 1b, 2c). Therefore, the next day she underwent a left surgical iridectomy (Figure 1c, 2d). Eight months on, she has remained stable with an IOP of 12 on no anti-glaucoma medication with a VA of 6/9.

The Mathematical Model

A mathematical model was constructed to determine the optimal size of PI required in patients with uveitis related iris bombe and angle closure (Figure 3a). To mimic the PS, the inner edge of the iris was assumed to be adhered to the lens, preventing flow of aqueous humour between the posterior and anterior chambers. As fluid accumulates in the posterior chamber, this drives a pressure difference (ΔP) across the iris and causes it to deform. The PI formed in the iris is modelled as a small cylindrical aperture of the radius r . For the system to be in equilibrium, the liquid flow through the PI must be matched exactly by the production flow Q of aqueous humour. Assuming the flux of liquid through the PI can be approximated by Poiseuille's law, it emerges that the transiris pressure difference can be written as $\Delta P = 8\eta hQ/(\pi r^4)$, where η is the viscosity of aqueous humour. This formula was used to determine the optimal radius r of the PI.

Results

Using the model parameters (Table 1), three typical examples of the iris shape for differing ΔP are shown in Figure 3b; as ΔP increases the iris bulges axissymmetrically into the anterior chamber, consistent with Figure 2b-d.

The simulations show that the angle between the iris and cornea, denoted as θ , decreases as the pressure difference across the iris increases, and for ΔP above a threshold, denoted ΔP_c , the iris makes contact with the cornea leading to acute angle closure (Figure 4a). For the model parameters, this critical pressure difference is calculated to be $\Delta P_c = 0.3871\text{mmHg}$ for the normal iris elastic properties. This value is slightly larger than the pressure differences assumed in other modelling studies^{1,4}. Decreasing the Young's modulus by a factor of 10 ($E = 0.96\text{ kPa}$), the critical pressure difference for this atrophic/floppy iris takes a much smaller value $\Delta P_c = 0.0385\text{mmHg}$.

The predicted curve of ΔP versus PI radius r (Figure 4b) shows the critical pressure difference between the anterior and posterior chambers decreases as the radius of the PI increases. The predicted minimal PI radius can be as large as $32.27\mu\text{m}$ for a normal iris. A ten-fold decrease in the Young's modulus of the iris as predicted in uveitic eyes, results in the critical area of the PI increasing by approximately a factor of three, predicting the minimal PI radius to be larger at $57.47\mu\text{m}$. In addition, variations in the viscosity of the aqueous demonstrate an increase in the critical area of the PI (Table 2).

Discussion

Uveitic glaucoma is a condition, first described in 1813 by Joseph Beer⁵, where ocular inflammation causes a persistent or recurrent elevation in intraocular pressure (IOP). It is relatively uncommon, however in chronic uveitis the prevalence can be as high as 46%⁶. Both secondary open angle and closure mechanisms are implicated, with a multi-factorial pathogenesis. Secondary angle closure glaucoma usually presents acutely and therefore requires immediate anti-glaucoma medical therapy to reduce the IOP. If the mechanism is pupil block, the standard practice is Nd:YAG PI. During episodes of uveitis, multiple mechanisms can increase the resistance to aqueous outflow leading to an elevated IOP.

In our case we believe multiple factors contributed to the development of AACG. She had damaged/scarred TM and 270° of PAS implying she had elements of both secondary open and closed angle glaucoma prior to having tube surgery. She went on to develop AACG on two occasions despite having a functioning tube. Both were due to the formation of 360° PS causing pupil block, iris bombe and resulting in occlusion of the Ahmed valve and angle closure in a pseudophakic eye. There are other factors in this case which we believe contributed to the failure of the Nd:YAG PI. The increased viscosity of the aqueous due to the chronic uveitis, increases the resistance in the aperture of the PI, reducing the flow through it. Coupled with a floppy, atrophic iris, the pressure required to cause the iris bombe was similar to blowing up a balloon. To blow a balloon initially a high amount of pressure is needed followed by minimal effort.

In our patient, despite a patent PI she developed AACG. The literature reports high failure rates in uveitis^{2,3}, however, the size of the PI is not determined in these studies. Furthermore, there are no reports in the literature documenting the average size of PI created by Nd:YAG, possibly as this is variable and often operator dependent.

Fleck et al, reported cases of primary AACG despite patent Nd:YAG PI, which have been thought to be due to inadequate size of PI¹. To determine the optimal size of PI required to prevent AACG, Fleck et al constructed a mathematical model which predicted a minimal size of iridotomy of 10-15 microns based on an estimate of the transiris pressure difference, which is difficult to measure *in vivo*. Their mathematical model was based on the assumptions of aqueous viscosity to be equal to the viscosity of water, aqueous flow rate = 2 µl/min and iris thickness of 50 microns. However, based on clinical case and experience, they recommended that the minimal size iridotomy required to prevent AACG should be at least 150-200 microns in diameter, incorporating a large safety margin.

In our patient, the size of the initial Nd:YAG PI was estimated to be 195 x 110 microns (Figure 1c), which suggests the a PI size greater than Fleck et al's recommendation of 150-200 microns is required in a uveitic eye. In our model, we improved on their approach by predicting the transiris pressure difference using computational solid mechanics. Assuming the viscosity of the aqueous in the eye to be the same as plasma and the iris stiffness to be comparable to a normal iris, the minimum diameter of PI predicted by our model is 64.56 microns. This critical value is significantly less than the YAG PI size used on our patient, explaining its initial success in reducing the patient's IOP. However, due to the ongoing pathology of the disease the IOP eventually increased again, and a further surgical PI was required to control the IOP. The model demonstrates that this further increase in IOP can be attributed to a decrease in the iris stiffness and/or an increase in the aqueous viscosity.

To account for changes in viscosity, we suggest a safety factor of three from the critical size predicted for a tenfold decrease in the iris stiffness ($E=0.96\text{kPa}$) and plasma aqueous viscosity of 1.6mPas , predicted as 114.96 microns. Therefore, in order to prevent AACG in patients with uveitis related iris bombe we recommend a diameter of PI of at least 300-350 microns. For a PI of the size 300 microns, this would be equivalent to 10 Nd:YAG PI of similar size to that conducted on our patient (195 x 110 microns). For a diameter of 350 microns this would equate to 20 Nd: YAG PIs.

The mathematical model constructed is deliberately simple and has limitations, with several of the model parameters, excluding the thickness of the iris, to be based on estimated values from the literature⁷⁻⁹. Parameters such as the aqueous viscosity and the iris stiffness and thickness will be dependent on the pathology of the disease and these values can only be estimated.

This case highlights the therapeutic challenge of managing a patient with uveitic glaucoma due to the complex relationship between IOP and inflammation. The construction a mathematical model allowed us to explore the possible mechanisms and variables in a uveitic eye. The model showed increasing aqueous viscosity and the atrophic/floppy properties of the iris, as postulated in a uveitic eye, requires a larger diameter of PI than previously recommended by Fleck et al of 150-200 microns. Based on our model, we suggest a minimum diameter of PI to be 300-350 microns to prevent AACG in a uveitic eye, suggesting a surgical approach rather than Nd:YAG PI may be more beneficial for these complex patients.

Word count: 1588

References

1. Fleck BW. How large must an iridotomy be? The British Journal of Ophthalmology. 1990; 74: 583-8
2. Spencer NA, Hall AJ, Stawell RJ. Nd:YAG laser iridotomy in uveitic glaucoma. Clinical & Experimental Ophthalmology. 2001; 29: 217-9
3. Schwatz LW et al. Neodymium-YAG laser iridectomies in glaucoma associated with closed or occludable angles. Am J Ophthalmol. 1986; 102:41-4.
4. J Heys, Barocas VH and Taravella MJ. Modeling Passive Mechanical Interaction Between Aqueous Humor and Iris. ASME J. Biomechanical Engineering 123:540-547, 2001.
5. Beer GJ. Die Lehre v. d. Augenkrankheiten. Vienna. 1813; 1:633
6. Netland PA, Denton NC. Uveitic Glaucoma. Contemp Ophthalmol 2006; 5:1-26
7. Heys J and Barocas VH. Mechanical characterization of the bovine iris. Journal of biomechanics, 1999, 32(9):999-1003.
8. Haidekker MA et al. A novel approach to blood plasma viscosity measurement using fluorescent molecular rotos. Am J Physiol Heart Circ Physiol. 2002; 282 (5): 1609-14
9. Kiel et al. Ciliary blood flow and aqueous humor production. Prog Retin Eye Res. 2011, 30(1): 1-17.
10. Lockington D et al. Mathematical and computer simulation modelling of intracameral forces causing pupil block due to air bubble use in descemet's stripping endothelial keratoplasty: the mechanics of iris buckling. Clinical & Experimental Ophthalmology. 2012, 40(2):182-186.

Figure Legends

Figure 1: Left eye slit lamp photograph showing:

- a) Corneal oedema, iris bombe, 360⁰ posterior synechiae, patent peripheral iridotomy and occluded Ahmed valve and IOP of 58mmHg
- b) Second peripheral iridotomy inferior to previous, occluded Ahmed valve, reduced iris bombe
- c) Broad surgical iridectomy (procedure: posterior synechiolysis, anterior vitrector used to create iridectomy at opening of the Ahmed valve with intracameral triamcinolone) and estimated size of first Nd:YAG PI

Figure 2: Imaging techniques were undertaken to investigate the mechanism of AACG:

- a) Left ultrasound biomicroscopy (UBM) showed marked iris bombe with the peripheral iris in contact with the cornea in all quadrants, very thin iris measuring approximately 0.3mm and the drainage tube at the 1 o'clock position showed the iris pointing up in to the tip of the tube occluding it
- b) Anterior segment optical coherence tomography (AS OCT) showed iris bombe, occlusion of drainage angle
- c) AS OCT Post YAG PI shows reduced iris bombe but there is still occlusion of drainage angle
- d) As OCT Post-surgical iridectomy shows flattened iris with open angle and resolved iris bombe

Figure 3: Mathematical Model:

- a) The geometry of the model has been scaled from the UBM image (Figure 2a): the iris modelled as a deformable elasticated disc with a central circular aperture¹⁰, the cornea and the lens are assumed to be rigid and impermeable
- b) Computations of the iris shape as a function of this transiris pressure difference were conducted in the Finite Element software ABAQUS 6.13 (SIMULIA, Providence, RI), assuming the iris to be of uniform initial thickness h with elastic moduli listed in Table 1. The elastic stiffness of the iris tissue is represented by its Young's modulus, E , and its compressibility by its Poisson ratio, ν . Three snapshots of the iris deformation as a function of the pressure difference ΔP . The black lines indicate the computational mesh used in simulations and the colour shading indicates the displacement in the iris tissue

Figure 4:

- a) ΔP vs θ : predicted acute angle between the cornea and the iris as a function of pressure difference for $E=9.6\text{kPa}$ and $E=0.96\text{kPa}$
- b) ΔP vs r : predicted radius of PI as a function of the pressure drop for $E=9.6\text{kPa}$ and $E=0.96\text{kPa}$ with corresponding prediction for $\eta=1.0\text{mPa s}$, 1.6 mPa s 3.0mPa s and 10.0mPa s

Tables

Table 1: Parameters used in the mathematical model.

Parameter	Symbol	Value
Young's modulus of normal iris	E	9.6 kPa^{15}
Young's modulus of atrophic/floppy iris	E	0.96 kPa
Poisson ratio of iris	ν	0.48
Thickness of iris	h	0.3mm
Viscosity of aqueous humour	η	1.6 mPa s^{16}
Production flux of aqueous humour	Q	$2.75\mu\text{l/min}^{17}$

Table 2: Minimal PI radius as a function of the viscosity of aqueous humour.

Young's modulus of iris, E (kPa)	Viscosity of aqueous humour, η (mPa s)	Critical pressure difference, ΔP_c (mmHg)	Minimal radius of PI, r (μm)	Minimal area of PI ($\times 10^3 \mu\text{m}^2$)
9.6	1.0	0.3871	28.69	2.58
	1.6		32.27	3.27
	1.8		33.24	3.47
	3.0		37.77	4.48
	10.0		51.03	8.18
0.96	1.0	0.0385	51.10	8.20
	1.6		57.47	10.37
	3.0		67.25	14.21
	10.0		90.88	25.94

Figures

Figure 1

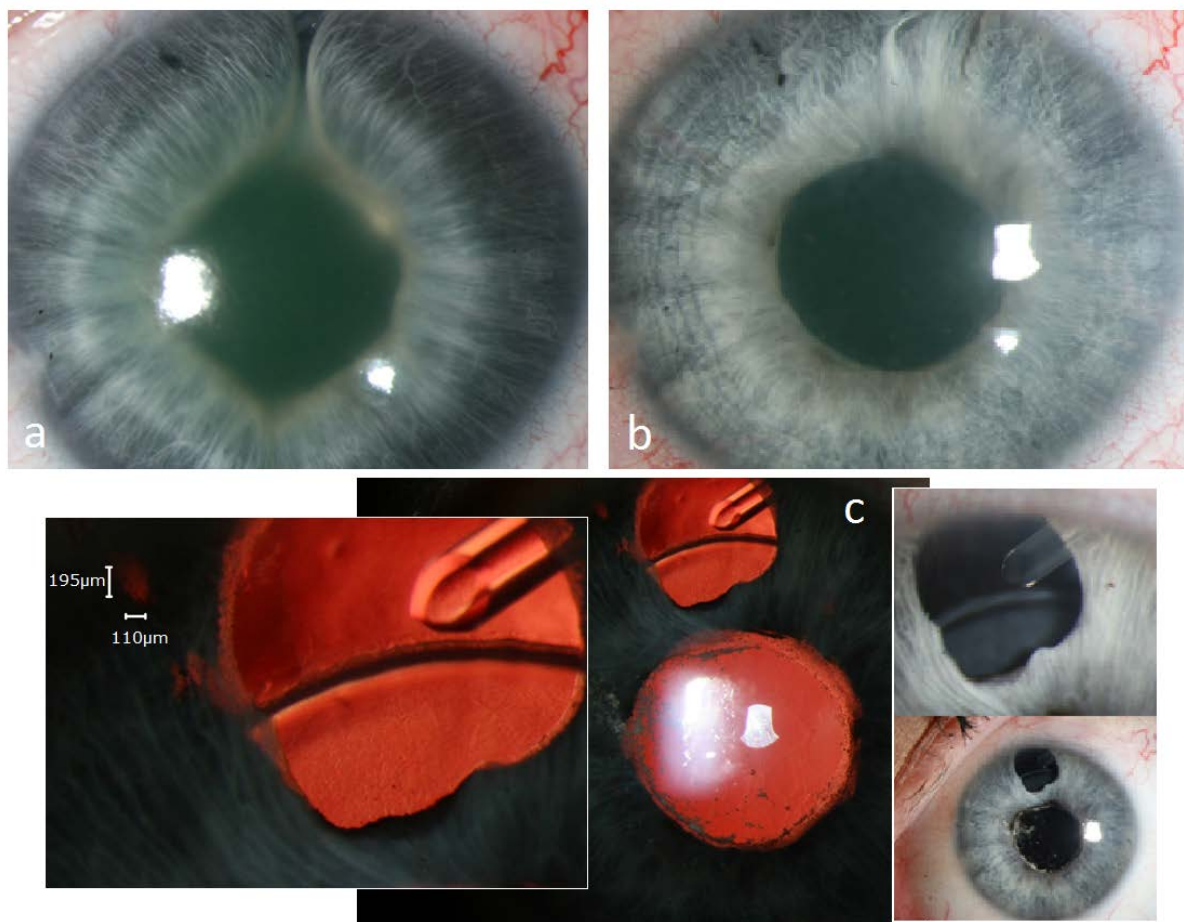


Figure 2

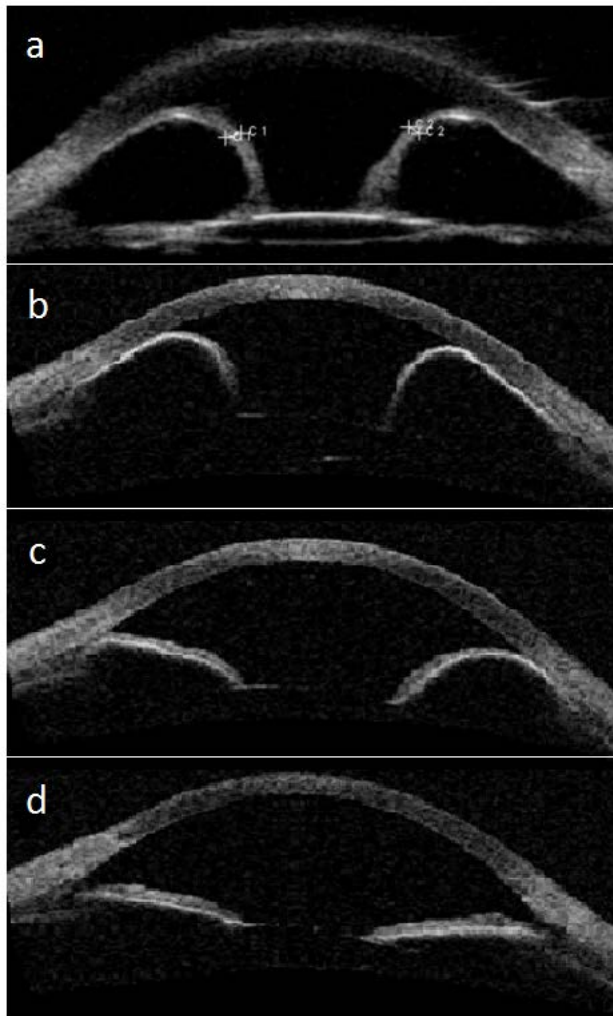


Figure 3

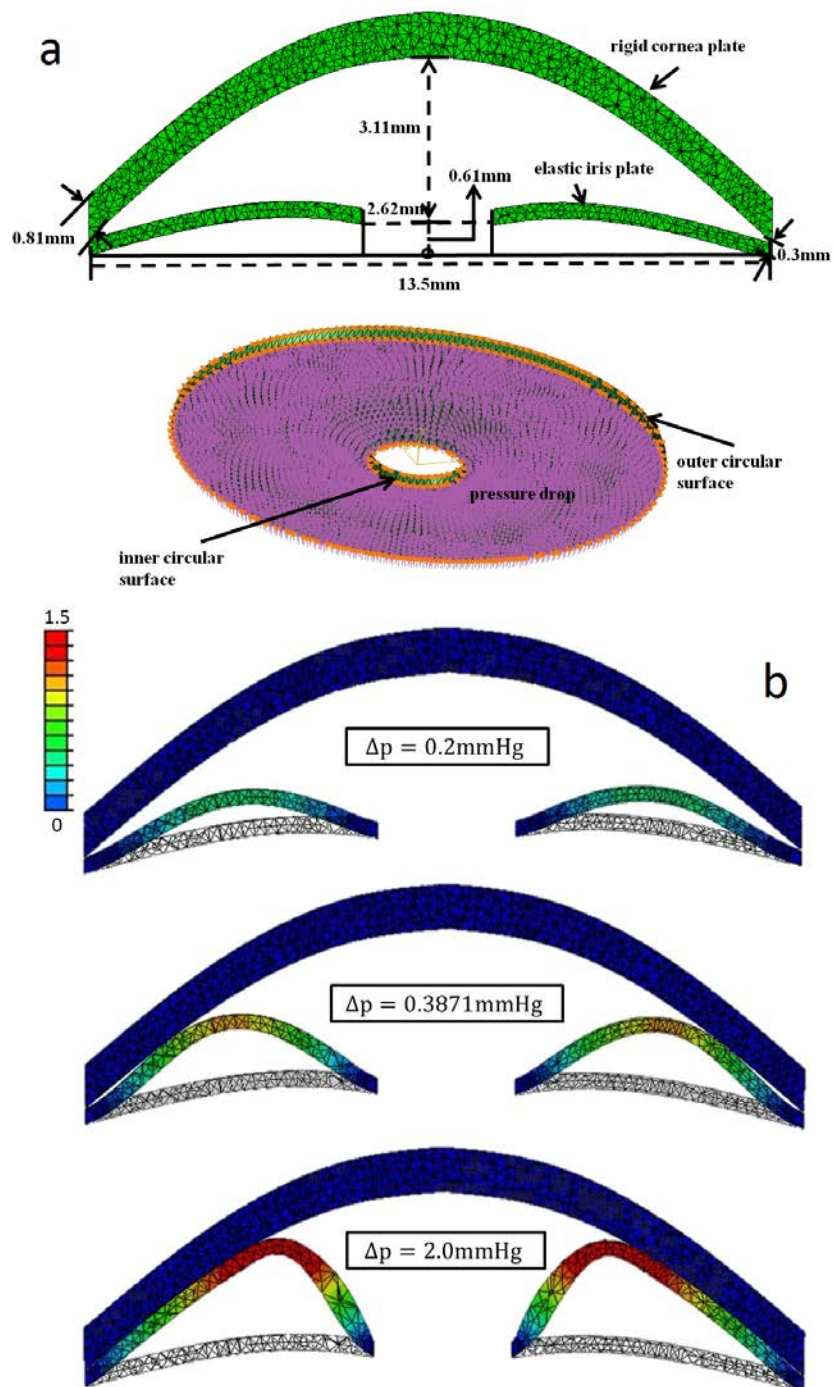


Figure 4

